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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-370]

Schedules of Controlled Substances: Placement of Alfaxalone into Schedule IV

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of Proposed Rulemaking.

SUMMARY: The Drug Enforcement Administration (DEA) proposes the placement of 5α-pregnan-3α-ol-11,20-dione (alfaxalone) including its salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible, into Schedule IV of the Controlled Substances Act (CSA). This proposed action is pursuant to the CSA which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking.

DATES: DEA will permit interested persons to file written comments on this proposal pursuant to 21 CFR 1308.43(g). Electronic comments must be submitted and written comments must be postmarked on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER]. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after midnight Eastern Time on the last day of the comment period.

Interested persons, defined at 21 CFR 1300.01 as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)," may file a

request for hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.45 and 1316.47. Requests for hearing and waivers of participation must be received on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: To ensure proper handling of comments, please reference "Docket No. DEA 370" on all electronic and written correspondence. DEA encourages all comments be submitted electronically through http://www.regulations.gov using the electronic comment form provided on that site. An electronic copy of this document and supplemental information to this proposed rule are also available at the http://www.regulations.gov website for easy reference. Paper comments that duplicate the electronic submission are not necessary as all comments submitted to www.regulations.gov will be posted for public review and are part of the official docket record. Should you, however, wish to submit written comments via regular or express mail, they should be sent to the Drug Enforcement Administration, Attention: DEA Federal Register Representative/OD, 8701 Morrissette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation must be sent to Drug Enforcement Administration, Attention: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: John W. Partridge, Executive Assistant, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, Virginia 22152; Telephone: (202) 307-7165.

SUPPLEMENTARY INFORMATION:

Posting of Public Comments: Please note that all comments received are considered part of the public record and made available for public inspection online at http://www.regulations.gov and in the DEA's public docket. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter.

If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be posted online or made available in the public docket, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all of the personal identifying information you do not want posted online or made available in the public docket in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be posted online or made available in the public docket, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify confidential business information to be redacted within the comment. If a comment has so much confidential business information that it cannot be effectively redacted, all or part of that comment may not be posted online or made available in the public docket.

Personal identifying information and confidential business information identified and located as set forth above will be redacted, and the comment, in redacted form, will be posted online and placed in the DEA's public docket file. Please note that the Freedom of Information Act applies to all comments received. If you wish to inspect the agency's public docket file in person by appointment, please see the "For Further Information Contact" paragraph, above.

Request for Hearing, Notice of Appearance at or Waiver of Participation in Hearing

In accordance with the CSA, this action is a formal rulemaking "on the record after opportunity for a hearing." 21 U.S.C. 811(a). Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (5 U.S.C. 556 and 557) and 21 CFR 1308.41.

Pursuant to 21 CFR 1308.44(a)-(c), requests for hearings, notices of appearances, and waivers of participation may be submitted only by interested persons, defined at 21 CFR 1300.01 as those "adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811)." Such requests or notices must conform to the requirements of 21 CFR 1308.44(a) or (b) and 1316.47 or 1317.48, as applicable. A request or notice should state, with particularity, the interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver must conform to the requirements of 21 CFR 1308.44(c) and 1316.49, including a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to 21 U.S.C. 811(a), the purpose and subject matter of the hearing is restricted to "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed…" Requests for hearing, notices of appearance at the hearing, and waivers of participation in the hearing should be submitted to DEA using the address information provided above.

Legal Authority

The DEA implements and enforces Titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, often referred to as the Controlled Substances Act and the Controlled Substances Import and Export Act (21 U.S.C. 801-971), as amended (hereinafter, "CSA"). The implementing regulations for these statutes are found in Title 21 of the Code of Federal Regulations (CFR), parts 1300 to 1321. Under the CSA, controlled substances are classified in one of five schedules based upon their potential for abuse, their currently accepted medical use, and the degree of dependence the substance may cause. 21 U.S.C. 812. The initial

schedules of controlled substances by statute are found at 21 U.S.C. 812(c) and the current list of scheduled substances are published at 21 CFR Part 1308.

The CSA permits these schedules to be modified by providing that scheduling of any drug or other substance may be initiated by the Attorney General: (1) on his own motion; (2) at the request of the Secretary of Health and Human Services (HHS); or (3) on the petition of any interested party. 21 U.S.C. 811(a). The Attorney General may, by rule, "add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed…" 21 U.S.C. 811(a). The findings required for the placement of a controlled substance in Schedule IV are: the drug or other substance has a low potential for abuse relative to the drugs or other substances in Schedule III; the drug or substance has a currently accepted medical use in treatment in the United States; and abuse of the drug or other substance may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule III. 21 U.S.C. 812(b)(4).

Background

Alfaxalone (5α-pregnan-3α-ol-11,20-dione, previously spelled alphaxalone), a substance with central nervous system (CNS) depressant properties, is a neurosteroid that is a derivative of 11-alpha-hydroxy-progesterone. A New Animal Drug Application (NADA) for alfaxalone, as an intravenous injectable anesthetic, was recently approved by the Food and Drug Administration (FDA) for the induction and maintenance of anesthesia and for induction of anesthesia followed by maintenance of anesthesia with an inhalant anesthetic, in cats and dogs. Alfaxalone primarily acts as an agonist at the gamma-aminobutyric acid (GABA) receptor-channel complex, with a

mechanism of action at this site similar to that of barbiturates like phenobarbital (Schedule IV) and methohexital (Schedule IV), benzodiazepines such as diazepam (Schedule IV) and midazolam (Schedule IV), as well as the anesthetic agents, propofol (Schedule IV under consideration) and fospropofol (Schedule IV).

Proposed Determination to Schedule Alfaxalone

Pursuant to 21 U.S.C. 811(a), proceedings to add a drug or substance to those controlled under the CSA may be initiated by request of the Secretary of HHS. On July 17, 2012, HHS provided DEA with a scientific and medical evaluation document prepared by FDA entitled "Basis for the Recommendation for Control of alfaxalone in Schedule IV of the Controlled Substances Act." Pursuant to 21 U.S.C. 811(b), this document contained an eight-factor analysis of the abuse potential of alfaxalone, along with HHS' recommendation to control alfaxalone under Schedule IV of the CSA.

In response, DEA conducted an eight-factor analysis of alfaxalone's abuse potential pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in the scheduling decision. Please note that both the DEA and HHS analyses are available in their entirety under "Supporting and Related Material" of the public docket for this rule at www.regulations.gov under docket number DEA-370.

1. The Drug's Actual or Relative Potential for Abuse: The abuse potential of alfaxalone is associated with its ability to evoke pharmacological effects similar to those evoked by the Schedule IV substances such as fospropfol, propofol (Schedule IV under consideration), and midazolam.

Since alfaxalone is a new veterinary product and has not been marketed in the United States, information on actual abuse of alfaxalone in the United States is not available. However, the

legislative history of the CSA offers another methodology for assessing a drug or substance's potential for abuse:

> The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.[1]

According to HHS, alfaxalone is thought to interact with the gamma-aminobutyric acid subtype A (GABA)-A receptors, and to enhance the activity of GABA, the principal inhibitory neurotransmitter in the central nervous system (CNS). This pharmacological evidence suggests that the abuse potential of alfaxalone is comparable to other drugs with a similar mechanism of action, and similar anesthetic properties, such as midazolam (Schedule IV), methohexital (Schedule IV), fospropofol (Schedule IV) and propofol (Schedule IV under consideration). Similar to the above mentioned Schedule IV sedative-hypnotics, alfaxalone acts as an inhibitor on the CNS and produces sedation and anesthesia. Based on the similarities between propofol and alfaxalone regarding their mechanisms of action and their intended routes of administration for clinical use, and the fact that 96% of propofol abuse reports involved abuse by medical professionals, HHS reasoned that alfaxalone abuse might be by medical professionals who have access to the drug and have knowledge in the intravenous administration of drugs.

There are no published studies of abuse potential for alfaxalone in humans. However, there is evidence that alfaxalone produces the sedative-hypnotic midazolam-like discriminative stimulus effects in rats and monkeys, as well as some ethanol-like effects

[1] Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970); 1970 U.S.C.C.A.N. 4566, 4601.

in rats. Based on the pharmacological similarities to other Schedule IV potent sedative-hypnotic drugs, such as midazolam, methohexital and fospropofol, the consequences of abuse of alfaxalone can be predicted to be similar to those drugs mentioned above. Furthermore, abuse and misuse of these drugs might result in death. The overt behavioral effects and adverse events produced by alfaxalone in animals are similar to those caused by Schedule IV benzodiazepines and barbiturates.

In summary, the relative abuse potential of alfaxalone can be considered no greater than the Schedule IV substances such as fospropfol, propofol, and midazolam and less than that of other sedatives in Schedule III.

2. Scientific Evidence of the Drug's Pharmacological Effects, If Known: According to the HHS review, alfaxalone acts directly through the GABA-A receptor-channel complex and increases the probability that the channel will enter into naturally-occurring open states of relatively long duration. The activity of alfaxalone on GABA receptors is similar to that of barbiturates like phenobarbital and methohexital (Schedule IV) as well as anesthetic agents like propofol (Schedule IV under consideration) and fospropofol (Schedule IV). Furthermore, similar to benzodiazepines such as diazepam and midazolam, alfaxalone can also increase the frequency of single channel openings. Additionally alfaxalone has been shown to inhibit T-type calcium channels. Alfaxalone does not affect cannabinoid (CB1 subtype), dopamine (D1-, D2-, D3-, D4- and D5- subtype), glutamate (AMPA, kainate, and NMDA subtype), opioid (mu, kappa and delta subtype), and serotonin (1A, 2B, 2C, 3, 5A and 6 subtype) receptors, nor does it affect the transporters for dopamine, norepinephrine and serotonin. In addition, alfaxalone does not significantly bind to major steroid nuclear receptors including androgens, estrogens, glucocorticoids or progesterone receptors.

Pre-clinical behavioral studies showed that, similar to chlordiazepoxide (Schedule IV), alfaxalone produces anxiolytic-like behavioral effects in rat models of anxiety, such as the elevated plus maze, the conflict test and restraint stress. In a published drug discrimination study, in which rats were trained to discriminate midazolam (Schedule IV) from saline, alfaxalone fully generalized to the midazolam discriminative cue. These results are consistent with previously published studies showing ethanol-like discriminative stimulus effects of alfaxalone and with other studies showing that other neurosteroids have barbiturate-like or benzodiazepine-like discriminative stimulus effects in rats and monkeys. This pharmacological profile of alfaxalone is consistent with neurosteroids with GABAergic effects.

According to the HHS review, the oral administration of alfaxalone as compared to its intravenous administration is 100 times less potent for producing midazolam-like effects. Alfaxalone has a low oral bioavailability (about 2%). It has been shown that an intravenous dose of about 50 mg of alfaxalone results in anesthesia in humans with a plasma level of 3 mg/L. Accordingly, an oral dose of about 2500 mg might be expected to result in anesthesia at the plasma level of 3 mg/L in humans, and thus oral doses of 250 to 800 mg of alfaxalone should be needed to produce a sub-anesthetic intoxication at plasma levels in a range of 0.3 to 1.0 mg/L. For a vial containing 100 mg of alfaxalone for an oral use, an amount of 2.5 to 8 vials would be needed to produce a “high”.

As stated in the HHS review, self-administration studies in animals with pregnanolone, allopregnanolone, endogenous metabolites of progesterone and a neuroactive steroid, Co 8-7071, showed that these substances produce some positive reinforcing effects in rats and rhesus monkeys. These substances, similar to alfaxalone, positively modulate GABA-A receptors by binding at the neurosteroid modulatory site. HHS stated that these data are predictive of abuse

potential of alfaxalone. HHS review also cited recent evidence that alpha4, beta3 and delta GABA-A receptors are modulated by both THDOC, a neurosteroid, and propofol. Based on this potential overlap in cellular targets, comparable kinetic profiles, and similar clinical indications for propofol and alfaxalone, HHS reasoned that alfaxalone may produce reinforcing effects similar to those of propofol.

In summary, alfaxalone, similar to chlordiazepoxide (Schedule IV), has anxiolytic activity in animals. Alfaxalone produced midazolam-like (Schedule IV) discriminative stimulus effects in rats, and it may share propofol's reinforcing effects. The abuse-related neuropharmacology profile of alfaxalone is similar to that of Schedule IV substances.

3. The State of Current Scientific Knowledge Regarding the Drug or Other Substance: The chemical name of alfaxalone is 5α-pregnan-3α-ol-11, 20-dione. Alfaxalone has a molecular formula of $C_{21}H_{32}O_3$ and a molecular weight of 332.5 g/mol, and a melting point of 165° to 171°C. Alfaxalone has a poor water solubility (< 5 μg/ml), but its water solubility increases to 80 mg/ml via complexation with cyclodextrins, especially 2-hydroxypropyl-beta-cyclodextrin (2HPCD). According to the HHS review, the alfaxalone product for veterinary anesthesia will be formulated as a 10 mg/ml solution of alfaxalone in 2HPCD (80 mg/ml), sodium phosphate buffer and water, adjusted to a pH of 6.5 to 7. According to the Sponsor's information cited by the HHS review, the processes involved in the synthesis and purification of alfaxalone are highly complex and require expertise in chemistry manufacture.

According to the HHS, the half-lives of alfaxalone are 24-37 and 45-77 minutes in dogs and cats, respectively. The clearance of alfaxalone is 59 ml/min/kg in dogs and 28 ml/min/kg in cats. The primary routes of elimination in the rat are biliary (65%) and renal (35%) routes. The half-life of alfaxalone in humans is about 35 minutes. The major metabolites in humans are

glucuronidated and the primary route of elimination is through renal (80%). Oral bioavailability of alfaxalone is about 2% as compared to its intravenous administration in humans. A clinical study showed that an intravenous administration of 30 mg alfaxalone produced plasma levels of about 3 mg/L, accompanied by anesthesia in humans. The veterinary alfaxalone product that is recently approved by the FDA contains 100 mg/vial (a vial of 10 ml formulated solution, 10 mg/ml of alfaxalone) which would be sufficient to produce anesthesia in two individuals when administered intravenously. HHS also states that because alfaxalone can be abused at subanesthetic doses, a 100 mg vial of alfaxalone drug product administered intravenously could be used repeatedly by the same individual, or by multiple individuals, who intended to abuse the substance.

4. Its History and Current Pattern of Abuse: Since alfaxalone is a new veterinary product and has not been marketed in the United States, information on actual abuse of alfaxalone in the United States is not available. Because alfaxalone has been marketed under the trade name Alfaxan® in the United Kingdom (UK) since 2007, the Sponsor submitted to HHS the results of a search of pharmacovigilance reports to the UK Veterinary Medicines Directorate. According to HHS, the Sponsor also provided information obtained from several other sources regarding diversion and abuse of alfaxalone. None of the above sources contained evidence of abuse of alfaxalone by humans. According to the HHS review, a search conducted by the Sponsor of the publically-available pharmacovigilance database provided by the UK's Medicines and Healthcare Products Regulatory Agency (MHRA) website also did not produce reports related to alfaxalone abuse. DEA conducted a comprehensive search of several major national drug abuse monitoring programs and found no evidence of alfaxalone abuse. It may be due to the fact that alfaxalone-containing products have not been marketed in the United States to date. However,

alfaxalone's pharmacological properties suggest that its pattern of abuse would be similar to other drugs used in maintenance and induction of anesthesia, such as midazolam (Schedule IV) and propofol (Schedule IV under consideration).

5. The Scope, Duration, and Significance of Abuse: As mentioned above, a comprehensive search by DEA of the major national drug abuse monitoring programs found no evidence of human abuse of alfaxalone in the U.S. However, as stated in the HHS review, the "suspicious order monitor system" of the U.S. distributor of alfaxalone, will be utilized to monitor the diversion of this product. This monitoring system of evaluates order quantities, buying patterns, and customer class regarding orders of unusual volume that could indicate diversion. As part of their monitoring, daily searches of the DEA website for new abuse issues and for abuse-related data from HHS's Substance Abuse and Mental Health Administration Services (SAMHSA) will be conducted. Additionally, the Sponsor will provide FDA with pharmacovigilance information for both animal and human adverse events from all markets.

6. What, if any, Risk There is to the Public Health: According to the HHS review, the public health risks of alfaxalone are mostly risks to the individual abuser and the risks are similar to those associated with the abuse of other sedative hypnotics and CNS depressants, such as midazolam and methohexital. Abuse of alfaxalone may lead to the death of the abuser or other adverse events that affect behavior, reaction ability and timing in operating a motor vehicle or machinery. As an anesthetic, the adverse events (AEs) that are likely to result from alfaxalone use are usually similar to those arising from the use of most general anesthetics. These events include apnea, bradycardia, bradypnea, hypertension, hypotension, hypothermia, hypoxia, unacceptable anesthesia quality, tachycardia and emesis. These AEs were found in animal

studies involving cats and dogs. Alfaxalone, as anesthetic product if used in excess, carries potential for overdose.

HHS cited two cases involving the accidental overdose of the alfaxalone human product, Althesin®, a human product containing combination of alfaxalone/alfadolone which was previously withdrawn from market. HHS stated that the occurrence of an accidental or purposeful overdose of Alfaxan® (containing 10 mg/ml of alfaxalone) is unlikely. HHS reasoned that if a person were trying to duplicate the same accidental overdose of injectable alfaxalone solution, he or she would be required to draw up a large volume of alfaxalone solution into the syringe. The intravenous self-administration of such large volume of Alfaxan® would be a very difficult if not impossible to perform, as the person would likely be anesthetized after the first 4.2 ml of the injection. If a person were to drink Alfaxan® to try to cause overdose, it would require 100 times more drug because of alfaxalone's poor oral bioavailability (1 - 2%). According to HHS, little is known about other health effects that might occur in someone abusing the drug chronically. In summary, the public health risks of alfaxalone abuse are similar to those associated with the abuse of other sedative hypnotics and CNS depressants, such as midazolam and methohexital which are controlled in Schedule IV of the CSA and propofol (Schedule IV under consideration). The major adverse events of these anesthetics include respiratory depression and deaths.

7. Its Psychic or Physiological Dependence Liability: According to HHS, studies of abrupt discontinuation of alfaxalone were not conducted. However, a study cited (McMohan et al., 2007) by the HHS review suggested the ability of alfaxalone to produce physical dependence. McMahon and his associates found that alfaxalone reduced the discriminative cue produced by flumazenil-precipitated withdrawal following chronic administration of benzodiazepines such as

diazepam or lorazepam (both Schedule IV) in Rhesus monkeys (McMahon et al., 2007). The HHS review concludes that alfaxalone can decrease withdrawal resulting from chronic administration of other positive GABA-A receptor modulators. According to HHS, there is no data available on the effects of abrupt discontinuation of alfaxalone because, as an anesthetic, it is not used chronically and not available for chronic use.

8. Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under the CSA: Alfaxalone is not considered an immediate precursor of any controlled substance of the CSA as defined by 21 U.S.C 802(23).

Conclusion: Based on consideration of the scientific and medical evaluation and accompanying recommendation of HHS, and based on DEA's consideration of its own eight-factor analysis, DEA finds that these facts and all relevant data constitute substantial evidence of potential for abuse of alfaxalone. As such, DEA hereby proposes to schedule alfaxalone as a controlled substance under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as Schedules I, II, III, IV, and V. The statute outlines the findings required to place a drug or other substance in any particular schedule. 21 U.S.C. 812(b). After consideration of the analysis and recommendations of the Assistant Secretary for Health of HHS and review of all available data, the Administrator of DEA, pursuant to 21 U.S.C. 812(b)(4), finds that:

(1) 5α-pregnan-3α-ol-11,20-dione (alfaxalone) has a low potential for abuse relative to the drugs or other substances in Schedule III;

(2) 5α-pregnan-3α-ol-11,20-dione (alfaxalone) has a currently accepted medical use in treatment in the United States. Alfaxalone was approved for marketing by FDA as a

veterinary anesthetic product for the induction and maintenance of anesthesia in cats and in dogs;

and

(3) abuse of 5α-pregnan-3α-ol-11,20-dione (alfaxalone) may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule III.

Based on these findings, the Administrator of DEA concludes that 5α-pregnan-3α-ol-11,20-dione (alfaxalone) including its salts, isomers and salts of isomers, whenever the existence of such salts, isomers, and salts of isomers is possible, warrants control in Schedule IV of the CSA (21 U.S.C. 812(b)(4)).

Requirements for Handling Alfaxalone

If this rule is finalized as proposed, alfaxalone would be subject to the CSA and the Controlled Substances Import and Export Act (CSIEA) regulatory controls and administrative, civil and criminal sanctions applicable to the manufacture, distribution, dispensing, importing and exporting of a Schedule IV controlled substance, including the following:

Registration. Any person who manufactures, distributes, dispenses, imports, exports, engages in research or conducts instructional activities with alfaxalone or who desires to manufacture, distribute, dispense, import, export, engage in research or conduct instructional activities with alfaxalone would need to be registered to conduct such activities pursuant to 21 U.S.C. 822 and 958 and in accordance with 21 CFR Part 1301.

Security. Alfaxalone would be subject to Schedule III-V security requirements and would need to be manufactured, distributed, and stored in accordance with 21 CFR §§ 1301.71, 1301.72(b), (c), and (d), 1301.73, 1301.74, 1301.75(b) and (c), 1301.76, and 1301.77.

Labeling and Packaging. All labels and labeling for commercial containers of alfaxalone which is distributed on or after the effective date of the finalization of this rule would need to be in accordance with 21 CFR 1302.03-1302.07, pursuant to 21 U.S.C. 825.

Inventory. Every registrant required to keep records and who possesses any quantity of alfaxalone would be required to keep an inventory of all stocks of alfaxalone on hand pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11. Every registrant who desires registration in Schedule IV for alfaxalone would be required to conduct an inventory of all stocks of the substance on hand at the time of registration.

Records. All registrants would be required to keep records pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, 1304.21, 1304.22, and 1304.23.

Prescriptions. Alfaxalone or products containing alfaxalone would be required to be distributed or dispensed pursuant to 21 U.S.C. 829 and in accordance with 21 CFR 1306.03-1306.06, 1306.08, 1308.09, and 1306.21-1306.27.

Importation and Exportation. All importation and exportation of alfaxalone would need to be done in accordance with 21 CFR Part 1312, pursuant to 21 U.S.C. 952, 953, 957, and 958.

Criminal Liability. Any activity with alfaxalone not authorized by, or in violation of, the CSA occurring on or after effective date of the finalization of this proposed rule would be unlawful.

Regulatory Analyses

Executive Orders 12866 and 13563

In accordance with 21 U.S.C. 811(a), this proposed scheduling action is subject to formal rulemaking procedures done "on the record after opportunity for a hearing," which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for

scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget pursuant to Section 3(d)(1) of Executive Order 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988

This proposed regulation meets the applicable standards set forth in Sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform to eliminate ambiguity, minimizes litigation, establish clear legal standards, and reduce burden.

Executive Order 13132

This proposed rulemaking does not preempt or modify any provision of State law; nor does it impose enforcement responsibilities on any State; nor does it diminish the power of any State to enforce its own laws. Accordingly, this rulemaking does not have federalism implications warranting the application of Executive Order 13132.

Executive Order 13175

This proposed rule will not have tribal implications and will not impose substantial direct compliance costs on Indian tribal governments.

Paperwork Reduction Act of 1995

This action does not impose a new collection of information under the Paperwork Reduction Act of 1995, 44 U.S.C. 3501-3521.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, 21 CFR Part 1308 is proposed to be amended to read as follows:

PART 1308— SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for 21 CFR Part 1308 continues to read as follows:

   Authority: 21 U.S.C. 811, 812, 871(b), unless otherwise noted.

2. Section 1308.14 is amended by redesignating paragraphs (c)(1) through (c)(53) as paragraphs (c)(2) through (c)(54) and adding a new paragraph (c)(1) as follows:

§ 1308.14 Schedule IV.

* * * * *

(c) * * *

(1) 5α-pregnan-3α-ol-11,20-dione (Alfaxalone) …….(**2731**)

* * * * *

March 15, 2013
Dated**:**

Michele M. Leonhart
Administrator

[FR Doc. 2013-06651 Filed 03/22/2013 at 8:45 am; Publication Date: 03/25/2013]